Paper No. 33

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte SCOTT A MINNICH, STEVEN A. LOBEL, GERALD SCHOCHETMAN, PETER FENG, and RICHARD MASSEY

Appeal No. 1997-2389
Application No. 07/987,233

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and ROBINSON, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 27 - 47, which are all of the claims pending in the application.

Claims 27, 29, and 43 are illustrative of the subject matter on appeal and read as follows:

27. A method for analyzing a liquid sample to quantitatively determine the presence of a specific microbe which comprises:

distributing a defined volume of a liquid sample as a number of equal volume aliquots into a number of receptacles each associated with membrane material so that the

microbe is randomly distributed on the membrane material associated with said receptacles,

filtering the aliquots to collect on the membrane material microbes contained in the liquid sample and

sequentially performing in a single assay

1. a first test to determine the presumptive presence of the specific microbe and to confirm the presence of the microbe, which first test comprises:

(a) contacting the membrane material with a selective [sic] medium permitting growth of the microbes collected, said medium including metabolizable substrates;

(b) incubating the membrane materials so that the microbes multiply;

(c) analyzing the medium for a metabolic by product which indicates the presumptive presence of the specific microbe to be determined and for the presence of another metabolic by-product which confirms the presence of said microbe; and

(d) removing the non-selective medium from the membrane material and

2. a second test to completely determine and quantify the presence of the microbe, which second test comprises:

(a) contacting the microbe collected on the membrane material with a predetermined amount of a detectable reagent specific for the microbe to be determined under conditions permitting formation of complexes between the reagent and the microbe and

(b) determining the amount of complex formed and thereby the amount of the specific microbe originally present in the liquid sample.

29. The method of claim 27 wherein the reagent is a polynucleotide complementary to a gene of the microbe.

43. A method for analyzing a liquid sample to quantitatively determine the presence of a viable specific microbe which comprises

distributing a defined volume of a liquid sample as a number of equal volume aliquots into a number of receptacles each associated with membrane material so that the microbe is randomly distributed on the membrane material associated with said receptacles,

filtering the aliquots [sic] to collect on the membrane material microbes contained in the liquid sample and

sequentially performing in a single assay

a first test to determine the presumptive presence of the specific microbe and to confirm the presence of the microbe, which first test comprises:

(a) contacting the membrane material with a non-selective medium permitting growth of the microbes collected, said medium including metabolizable substrates;

(b) incubating the membrane material so that the microbes multiply;

(c) analyzing the medium for a metabolic by-product which indicates the presumptive presence of the viable specific microbe to be determined and for the presence of another metabolic by-product which confirms the presence of said viable microbe; and

(d) removing the non-selective medium from the membrane material and

a second test to completely determine and quantify the presence of the microbe, which second test comprises:

(a) contacting the microbe collected on the membrane material with a predetermined amount of a detectable immunoreactive reagent specific for the microbe to be determined under conditions permitting formation of complexes between the immunoreactive reagent and the microbe,

(b) completing the identification of the microbe based on said complex and

(c) determining the amount of complex formed and thereby the amount of the specific microbe originally present in the liquid sample.

The references relied upon by the examiner are:

Sadowski	4,443,549	Apr. 17, 1984
Fernwood et al. (Fernwood)	4,493,815	Jan. 15, 1985
Mattiasson	4,592,994	Jun. 3, 1986
Jolley	4,652,533	Mar. 24, 1987

Feng et al. (Feng), "Fluorogenic Assays for Immediate Confirmation of Escherichia Coli," Applied and Environmental Microbiology, Vol. 43, No. 6, pp. 1320-1329 (1982).

Singer et al. (Singer), "Optimization of in situ Hybridization Using Isotopic and Non-Isotopic Detection Methods," BioTechniques, Vol. 4, No. 3, pp. 230-243 (1986).

Grounds of Rejection

Claims 27, 28, 31 - 35, 43, and 47 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Jolley, Fernwood, and Mattiasson.

Claims 29, 30, 36 - 42, and 44 - 46 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Jolley, Fernwood, Mattiasson, Feng, Sadowski, and Singer.

Discussion

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims and to the respective positions articulated by the appellants and the examiner. We make reference to the Examiner's Answer (Paper No. 31) for the examiner's reasoning in support of the rejections and to the appellants' Appeal Brief (Paper No. 30) for the appellants' arguments thereagainst.

Background

Appellants describe the invention at pages 4-5 of the specification as being directed to a method for analyzing a liquid sample to determine the presence of a specific microbe, e.g., E. Coli wherein a known volume of a liquid sample is distributed into receptacles having a membrane present therein. The microbes are collected on the membrane and the membrane is contacted with a non-selective medium in order to permit the growth of any microbes isolated from the sample. The membrane material is then tested for one or more substances indicative of the presence of the microbe. The membrane bound microbes are then contacted with a solution containing a detectable reagent specific for the microbe under conditions permitting formation of a complex between the reagent and the microbe. Detection of the amount of complex formed permits determination of the amount of microbe originally present in the liquid sample.

The rejections under 35 U.S.C. § 103

In rejecting claims 27, 28, 31 - 35, 43, and 47 under 35 U.S.C. § 103, the examiner relies on Jolley as disclosing a method for quantitative determination of cellular antigens, including bacteria, wherein a liquid sample is inoculated into a number of receptacles having a membrane material present therein which permits the collection of the cells present in the sample. The bacteria on the membrane are contacted with a luminescent reagent specific for the bacteria and the amount of the microbe is determined by

determining the amount of complex formed. (Answer, page 6). The examiner acknowledges that Jolley (id.):

> lacks the insertion of an incubation period in non-selective medium to permit multiplication of bacteria in the receptacles and analysis of metabolic by-products . . . .

The examiner relies on Mattiasson and Fernwood to supply that which is missing from Jolley. Specifically, the examiner relies on Mattiasson as describing a method for quantifying the amount of organisms in a sample wherein the sample is placed in a receptacle associated with a membrane. The cells, of interest in the sample, are bound to the membrane using biospecific binding, such as a bound antibody specific to the cells or organism of interest. (Id.) Thus, Mattiasson uses the specific binding which binds the organism to the membrane as the qualitative test to ascertain the presence of a specific cell or organism rather than the determination of two or more metabolites resulting from the culturing step which Mattiasson uses for the quantitative step of the assay. The examiner cites Fernwood as describing a general method and apparatus for biochemical testing and screening wherein the receptacles are associated with a membrane in a system which permits multiple biochemical tests to be run simultaneously or sequentially. (Answer, paragraph bridging pages 6-7). Thus, the membrane permits the growth, secretion of cellular material in to the media, testing of the media and removal of the media and further testing of the cells remaining on the membrane after filtration.

The examiner concludes that (Answer, page 7):

> it would have been obvious for one of ordinary skill in the art to insert [the] Mattiasson's incubation period and metabolic determination into Jolley's immunodetermination method (between the initial inoculation and addition of the biospecific reagent) because Fernwood teaches cell growth in the receptacle prior to filtration through and retention on the membrane while Mattiasson teaches the specific metabolic assay steps of the instant invention; further, one of skill in the art would have known that the multiplication of organisms in the sample would increase the amount of analyte for detection. Moreover, it would have been obvious to subject the sample to preliminary biochemical testing or screening (as taught by Mattiasson) to identify samples warranting further characterization by highly specific, costly immunoreagents because Fernwood teaches that the same sample can be contacted with a series of reagents by contacting the sample with a reagent and drawing unreacted reagent through the membrane while retaining the sample on the membrane for further analysis.

The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicants. Id. In order to meet that burden the examiner must provide a reason, based on the prior art, or knowledge generally available in the art as to why it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 297, n.24, 227 USPQ 657, 667, n.24 (Fed. Cir. 1985,. cert. denied, 475 U.S. 1017 (1986).

On the record before us, we find that the facts and evidence provided by the examiner falls short of that which would have reasonably suggested to one of ordinary skill in this art at the time of the invention to modify the assay of Jolley in a manner to arrive at

the claimed assay. Essentially, the present claimed assay requires a qualitative step wherein the microbes which may be present in the sample are collected on a membrane and that membrane is contacted with a non-selective medium to permit growth of the microbes present. The medium is then analyzed for a metabolic product which indicates the presence of the specific microbe to be determined and for the presence of another metabolic by-product which confirms the presence of said microbe. Only then is the sample subjected to a quantitative assay to determine the amount of the specific microbe originally present in the liquid sample. It is not questioned that Jolley describes an assay which reasonably corresponds to the second assay step of the claims on appeal. However, Jolley does not describe or suggest the use of a qualitative assay to be preformed prior to the quantitative step. While Mattiasson may be read to describe a qualitative step prior to the quantitative step, that qualitative step relies on the specific binding of the microbe to a membrane. The subsequent culturing and determination of the metabolites associated with the culturing of the microbes bound to the membrane is performed not to confirm the presence of the microbes,
but to determine the amount of microbe present in the sample. Mattiasson is not concerned with detecting the presence of metabolic by-products which indicates the presence of the specific microbe to be determined. Thus, in order to arrive at the claimed invention starting with Jolley, one would first have to add a qualitative step involving a culturing of the microbes distributed on the membrane and then assaying the medium after

culturing for a metabolic by-product which would indicate the presumptive presence of the specific microbe to be determined. While Mattiasson might be read to suggest the use of a qualitative step prior to the quantitative analysis, Mattiasson does not suggest the use of the detection of the metabolic products from the culturing step as a qualitative step in an assay. Since Mattiasson has already established by binding of the microbes to the membrane, the presumptive presence of the microbe of interest, there is no need for Mattiasson to select those specific metabolites which would indicate the presence of the specific microbe to be determined. (Compare Mattiasson, column 3, line 60 - column 4, line 68).

Fernwood does not provide that which is missing from the disclosures of Jolley and Mattiasson. While Fernwood provides an apparatus which includes a receptacle which includes a membrane, wherein more than one biochemical process could be preformed, there is nothing which would have suggested that one should modify the methodology of Jolley, even with the teaching of Mattiasson, in a manner to arrive at the claimed invention.

With regard to the presently claimed method of analyzing a liquid sample to quantitatively determine the presence of a specific microbe, the examiner has not met the initial burden of establishing why the prior art, relied on, would have led one of ordinary skill in this art to arrive at the claimed assay. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir.1988). Therefore, the rejection of claims 27, 28, 31 - 35, 43, and 47 under 35 U.S.C. § 103 over the combination of Jolley, Fernwood, and Mattiasson is reversed.

In rejecting claims 29, 30, 36 - 42, and 44 - 46 under 35 U.S.C. § 103 the examiner has relied upon Jolley, Fernwood, and Mattiasson taken in further view of Feng, Sadowski, and Singer. We have noted the deficiencies of Jolley taken in combination with Fernwood and Mattiasson as their disclosure relates to the claimed invention. On consideration of this rejection under 35 U.S.C. § 103, we need only determine whether Feng, Sadowski, and Singer, additionally relied on in the rejection of claims 29, 30, 36-42 and 44-46, provide that which is lacking from the combined teachings of the other references. They do not.

At page 10 of the Examiner's Answer the examiner acknowledges that Jolley, Fernwood, and Mattiasson "differ from the instant invention in that they fail to disclose hybridization probes as the specific reagents in the second part of the assay" and "fail to disclose reagents specific for the determination of E.coli or other coliform bacteria." The examiner cites Sadowski to demonstrate that "it is conventional to detect E. coli with ani-pilar [sic] or antiflagellar monoclonal antibodies." (Answer, page 10). The examiner cites Feng to "show that determination of E. coli by metabolism of 4-methyl-umbelliferone-D-glucuronide is also conventional" and cites Singer "to show that it is conventional to detect specific microorganisms by in situ hybridization using polynucleotide probes." Thus, Sadowski, Feng, and Singer describe aspects of the rejected claims which are missing from the disclosures of Jolley, Fernwood, and Mattiasson, but fail to provide the suggestion or direction which would have led one of ordinary skill in this art to modify the methodology

of Jolley in a manner to arrive at the assay of the appealed claims. Therefore, even when the combined teachings of all of the references are considered, it remains that the examiner has failed to provide that evidence which would have led one of ordinary skill to modify the assay procedure of Jolley in a manner which would have resulted in the claimed invention. Therefore, the examiner has failed to establish a prima facie case of obviousness within the meaning of 35 U.S.C. § 103. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, supra. Therefore, the rejection of claims 29, 30, 36 - 42, and 44 - 46 under 35 U.S.C. § 103 is reversed.

Summary

The rejection of claims 27, 28, 31 - 35, 43, and 47 under 35 U.S.C. § 103 as unpatentable over the combination of Jolley, Fernwood, and Mattiasson is reversed. The rejection of claims 29, 30, 36 - 42, and 44 -46 under 35 U.S.C. § 103 as unpatentable over

the combination of Jolley, Fernwood, Mattiasson, Feng, Sadowski, and Singer is reversed.

REVERSED

SHERMAN D. WINTERS Administrative Patent Judge	))))) BOARD OF PATENT
WILLIAM F. SMITH Administrative Patent Judge	)) APPEALS AND)) INTERFERENCES
DOUGLAS W. ROBINSON Administrative Patent Judge	))

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